REMARKS

Claims 1, 4, 52, 64-69, and 85-113 are pending in the application. No amendments have been made by the present response.

Statement Concerning Common Ownership

Application serial number 09/909,460 and U.S. Patent No. 5,783,567 were, at the time the currently claimed invention was made, owned by, or subject to an obligation of assignment to, Pangaea Pharmaceuticals, Inc. All of the inventors of U.S. Patent No. 5,783,567 assigned their rights in the patent to Pangaea Pharmaceuticals, Inc. in an assignment recorded in the U.S. Patent & Trademark Office on August 18, 1997, at Reel 8672, Frame 0675. All of the inventors of Application serial number 09/909,460 assigned their rights in the application to Pangaea Pharmaceuticals, Inc. in an assignment recorded in the U.S. Patent & Trademark Office on September 13, 1999, at Reel 010225, Frame 0212. Application serial number 09/909,460 and U.S. Patent No. 5,783,567 were both subsequently assigned to and are currently commonly owned by Eisai Inc.

35 U.S.C. § 103(a) (Hedley et al. in view of Balland)

At page 2 of the Advisory Action, the final rejection of claims 1, 4, 52, 63-69, and 85-113 over Hedley et al., U.S. Patent No. 5,783,567 in view of Balland (1996) NATO ASI Series 290:131-42 was maintained. As established in the section above entitled "Statement Concerning Common Ownership," Application serial number 09/909,460 and U.S. Patent No. 5,783,567 were, at the time the currently claimed invention was made, owned by, or subject to an obligation of assignment to the same entity (Pangaea Pharmaceuticals, Inc.). Because U.S. Patent No. 5,783,567 was cited as prior art under 35 U.S.C. § 102(e) in the present 35 U.S.C. § 103(a) rejection, the statement of common ownership disqualifies the reference as prior art under 35 U.S.C. § 103(c). As a result, applicants request that the Examiner withdraw the rejection.

35 U.S.C. § 103(a) (Papahadjopoulos et al. in view of Cleek et al.)

At page 2 of the Advisory Action, the final rejection of claims 1, 4, 52, 63-69, and 85, 86, and 88-113 over Papahadjopoulos et al., U.S. Patent No. 6,210,707 ("the '707 patent") in view of Cleek et al. (1997) J. Biomed. Materials Res. 35:525-30 ("Cleek") was maintained.

The Advisory Action acknowledged that the claims are entitled to the priority date of January 22, 1998, but asserted that Papahadjopoulos et al., U.S. Patent No. 6,071,533 ("the '533 patent"), which was filed on November 10, 1997 (and to which the '707 patent claims priority as a continuation-in-part), renders the claims obvious when combined with Cleek. In particular, the Advisory Action stated that the '533 patent discloses "lipidic:nucleic acid complexes further complexed with polymers" and Cleek discloses "microparticles comprised of nucleic acid and PLGA, which appears to satisfy the limitation that the polymers have a solubility of less than about 1 mg/ml."

Applicants respectfully traverse the rejection in view of the following remarks.

Independent claim 1 is directed to a microparticle that is less than about 20 microns in diameter and contains: (i) a polymeric matrix consisting essentially of one or more synthetic polymers having a solubility in water of less than about 1 mg/l; (ii) a lipid; and (iii) a nucleic acid molecule. Independent claim 52 is directed to a preparation of microparticles, at least 90% of which have a diameter less than about 100 microns, wherein each of the microparticles comprises a polymeric matrix consisting essentially of one or more synthetic polymers having a solubility in water of less than about 1 mg/l, a nucleic acid, and a lipid.

In contrast, the lipid:nucleic acid complexes of the '533 patent contain, among other components: (a) a cationic lipid; (b) a nucleic acid; and (c) a ***hydrophilic*** polymer. The '533 patent specifically refers to the inclusion of a "hydrophilic polymer" in its complexes, and not merely a "polymer" as suggested in the final Office Action and the Advisory Action. The '533 patent defines a "hydrophilic polymer" as a "long chain highly hydrated flexible neutral polymer[] attached to lipid molecules" (the '533 patent at column 6, lines 27-30). According to the '533 patent, "the hydrophilic polymer locates and is incorporated into hydrophobic pockets in the complex via its hydrophobic side chains, while leaving the hydrophilic part at the exterior

surface, thereby stabilizing the entire complex" (the '533 patent at column 8, lines 35-39). PLGA, a copolymer composed of lactic acid and glycolic acid, *is not a "hydrophilic polymer" according to the meaning of the term as used in the '533 patent.* Because PLGA is not a "hydrophilic polymer," the skilled person clearly would have had no reason to substitute PLGA for the "hydrophilic polymer" component in the lipid:nucleic acid complexes described in the '533 patent. Hence, the combination of the '533 patent and Cleek does not render obvious the claimed microparticles.

Moreover, the claimed microparticles contain a polymeric "matrix" (i.e., a material in which something is enclosed or embedded) and not merely a "polymer." In contrast, the hydrophilic polymer used in the lipid:nucleic acid complexes of the '533 patent does not form the claimed "polymeric matrix." As noted in the preceding paragraph, the '533 patent states that the hydrophilic polymer is incorporated into hydrophobic pockets in the lipid:nucleic acid complex, leaving the hydrophilic part at the exterior surface. According to the '533 patent, "this invention relies on the unexpected discovery that a lipid:nucleic acid complex, which is mixed with a hydrophilic polymer after lipid:nucleic acid complex formation, exhibits high transfection activity and increased shelf life, as measured by transfection activity after storage" (the '533 patent at column 16, lines 58-62; emphasis added). A hydrophilic polymer that is mixed with a lipid:nucleic acid complex after it has been formed and incorporates into hydrophobic pockets in the complex, as is disclosed in the '533 patent, would not form a "polymeric matrix" as is required by the claims. Because the '533 patent does not contain a "polymeric matrix" as required by the claimed microparticles, substitution of a "hydrophilic polymer" of the '533 patent with *any* alternate polymer after lipid:nucleic acid complex formation (as is taught in the '533 patent) would not have resulted in the claimed microparticles.

In view of the foregoing comments, applicants respectfully submit that the cited references do not render obvious any of claims 1, 4, 52, 63-69, and 85, 86, and 88-113. Applicants request that the Examiner withdraw the rejection.

CONCLUSION

Applicants submit that all grounds for rejection have been overcome and that all claims are in condition for allowance, which action is requested.

Enclosed is a Petition for Extension of Time. The extension of time fee is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply any deficiencies or credit any overpayment to deposit account 06-1050, referencing Attorney Docket No. 08190-014002.

Respectfully submitted,

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